bacterial infections. Prospective, randomized clinical trials of both prophylactic and therapeutic transfusions have been recently completed. It has been found that HLA matched prophylactic granulocyte transfusions decrease the incidence of bacterial infection developing in patients with neutropenia who are receiving bone marrow transplants; however, it has not been found to be any better than laminar air flow isolation. In non-HLA matched transfusions, however, the incidence of alloimmunization against leukocyte antigens severely limits its prophylactic use. In several therapeutic trials involving neutropenic patients with acute leukemia and aplastic anemia, transfused patients appeared to fare better than nontransfused patients; although, in some studies the differences were not statistically significant. This is due to variability in the types and amounts of granulocytes transfused in the different studies. Transfusions were of no benefit in patients with "fevers of undetermined origin" or in patients with neutrophil counts of over 1,000 per μl. The efficacy of granulocyte transfusion was directly related to the ability of the product to raise the granulocyte count in the recipient, so that smaller patients, or those given large daily or twice daily transfusions were more likely to benefit. In considering this form of therapy, two points should be noted. First, although some patients' conditions clearly improve with therapy, no studies have shown a definite increase in survival rates for patients receiving granulocyte transfusion. Second, no benefit is achieved in recipients for whom results of bone marrow examinations would predict recovery of neutropenia within three to five days. Granulocyte transfusions probably are most effective in causing improvement or cure of clinical infection when used in the following circumstances: (1) The patient has documented serious bacterial infection that remains unresponsive after 24 to 48 hours of parenteral broad spectrum antibiotic treatment, (2) the patient's neutrophil count is less than 500 per μl, with absent neutrophil precursors in the marrow, (3) healthy compatible donors, equipment and personnel for long-term support are available and (4) the patient has a good prognosis if recovery from the infection is obtained.

In spite of good evidence that granulocyte transfusions can alter the clinical course of serious bacterial infections in some patients with neutropenia, the modest overall benefit and inconvenience of daily procurement dictate that this therapy in general clinical practice should be reserved for selected patients.

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Progress Toward Effective Antiviral Agents

WHILE MANY VIRAL INFECTIONS are associated with illness and loss of work, serious consequences from such infections are unusual. However, aggressive treatment of diseases such as neoplasia or renal failure often involves therapies that alter the immune system and predispose patients to more serious viral infections. Thus, progressive viral diseases in immunosuppressed patients and occasional severe infections in otherwise healthy persons have served as incentives to the development of effective antiviral compounds. Recent events have suggested that such therapy exists. Three distinct substances have proved effective against viral infections when used in other than topical applications.

Amantadine is known to be an effective prophylactic agent when used to prevent infections with influenza A. This drug appears particularly useful in patients with serious underlying diseases who are exposed to outbreaks of influenza caused by this strain before immunization can be expected to produce reasonable antibody titer. Amantadine also appears of therapeutic value after the first symptoms of influenza have developed. However, its usefulness in this regard may be limited, and no information is available to suggest whether it is effective against influenzal pneumonia, the most hazardous complication.

Adenine arabinoside, a relatively new agent, has proved of definite benefit in patients with encephalitis due to herpes simplex virus, and has been effective in reducing mortality. In addition, adenine arabinoside may be effective in herpes zoster

and disseminated herpes infections in newborn infants.

Interferon, a natural body protein, has been produced in vitro in quantities sufficient for administration to patients and has been found effective against herpes zoster. However, it remains both difficult and expensive to produce.

In addition to the parenteral drugs mentioned, idoxuridine has long been an effective topical therapy for treatment of certain forms of herpetic keratitis, and topical adenine arabinoside appears even more beneficial in ocular disease.

Newer agents with considerable promise are being tested. They include acycloguanosine (Acyclovir), which is much more effective in vitro than adenine arabinoside against herpes viruses, and the glucose derivative 2-deoxy-D-glucose, which has been reported to be beneficial for genital herpes infections when applied topically.

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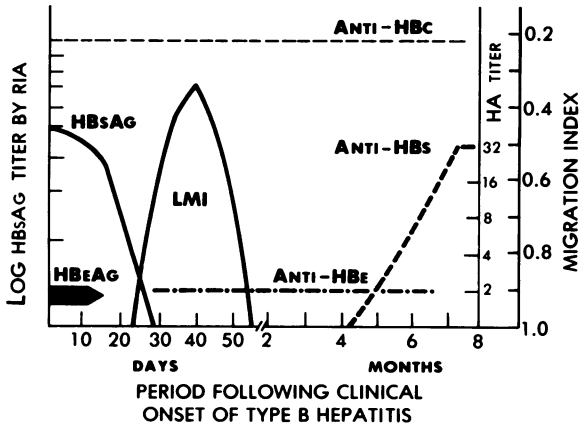
Immunodiagnosis of Viral Hepatitis

LABORATORY DIAGNOSIS OF HEPATITIS types A, B and non-A/non-B (abbreviated HA, HB and NANB, respectively) can be established by testing immunologic responses to the viral agents of HA and HB; NANB is established only by exclusion (Table 1).

In HA, the presence of anti-HA in the IgM class of immunoglobulins suggests a current or recent infection, whereas anti-HA appearing in the IgG class indicates infection occurring in the past and confers immunity to HA.



Anti-HBc = hepatitis B core antibody; Anti-HBe = hepatitis B "e" antibody; Anti-HBs = hepatitis B surface antibody; HBeAg = hepatitis B "e" antigen; HBsAg = hepatitis B surface antigen; RIA = radioimmunoassay.

Figure 1.—Immunologic response to HBsAg, HBcAg and HBeAg during acute and convalescent phases of type B hepatitis. The fact that leukocyte migration inhibition (LMI) with purified HBsAg is present but disappears after about four weeks suggests that hepatitis B virus infection may be self-limited. In contrast, the LMI test is negative in persistent or chronic cases of hepatitis B.

The temporal changes in various markers during the acute phase of HB are shown in Figure 1. Although the clinical manifestations of acute HA, HB or NANB are similar, a chronic carrier state and chronic liver disease of more than six months duration are recognized only for infection with HB or NANB agents. Nearly 10 percent of patients with acute HB have unresolved hepatitis, frequently persisting for years, and often progressing to a

TABLE 1.—*Practical Guide for the Interpretation of Serologic Markers of Viral Hepatitis*

Clinical Interpretation	*IgM Anti-HA**	*HBsAg*	*HBeAg*	*Anti-HBe*	*Anti-HBc*	*Anti-HBs*
Acute HA	+	−	−	−	−	−
Incubation period or early acute HB	−	+	+	−	−	−
Acute HB	−	+	+	−	+	−
Fulminant HB	−	+	−	−	+	+/−
Convalescence from acute HB	−	−	−	+	+	+/−
Chronic HB	−	+	+/−	+/−	+	+/−
Persistent HB carrier state	−	+	−	+	+	−
Past infection with HB virus	−	−	−	−	+	+
Infection with HB virus without detectable (excess) HBsAg	−	−	−	−	+	−
Immunization without infection	−	−	−	−	−	+
Non-A/non-B hepatitis by exclusion of markers for HA and HB	−	−	−	−	−	−

Anti-HA = hepatitis A antibody; HBsAg = hepatitis B surface antigen; HBeAG = hepatitis B "e" antigen; anti-HBe = hepatits B "e" antibody; anti-HBc = hepatitis B core antibody; anti-HBs = hepatitis B surface antibody.

*Clinically unrecognized infection occurring in childhood accounts for the high incidence of IgG anti-HA antibodies in 80 percent to 90 percent of adults in underdeveloped countries as compared with 25 percent to 50 percent of adults in Europe and the United States.